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DOI:

[10.1111/add.13946](https://doi.org/10.1111/add.13946)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Meier, M. H., Caspi, A., Danese, A., Fisher, H., Houts, R., Arseneault, L., & Moffitt, T. E. (2018). Associations between adolescent cannabis use and neuropsychological decline: a longitudinal co-twin control study. *Addiction*, 113(2), 257-265. <https://doi.org/10.1111/add.13946>

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Associations between Adolescent Cannabis Use and Neuropsychological Decline:
A Longitudinal Co-Twin Control Study

Madeline H. Meier, Ph.D.¹, Avshalom Caspi, Ph.D.,^{2,3,4} Andrea Danese, M.D., Ph.D.,^{4,5,6} Helen
L. Fisher, Ph.D.,⁴ Renate Houts, Ph.D.,^{2,3} Louise Arseneault, Ph.D.,⁴ & Terrie E. Moffitt,
Ph.D.^{2,3,4}

1. Department of Psychology, Arizona State University, Tempe, AZ, USA
2. Department of Psychology and Neuroscience, Duke University, Durham, NC, USA
3. Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, USA
4. Medical Research Council Social, Genetic, and Developmental Psychiatry Centre, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, UK
5. Department of Child and Adolescent Psychiatry, Institute of Psychiatry, Psychology, and Neuroscience, King's College London, UK
6. National and Specialist Service Foundation Trust, London, UK

Corresponding author: Madeline H. Meier, Department of Psychology, Arizona State University, PO Box 871104, Tempe, AZ 85287-1104. Email: madeline.meier@asu.edu. Phone: 480-727-2718. Fax: 480-965-8544.

Acknowledgements: The E-Risk Study is funded by the Medical Research Council (UKMRC grant G1002190). Additional support was provided by NICHD grant HD077482 and by the Jacobs Foundation. Dr. Fisher is supported by the MQ: Transforming Mental Health Fellowship MQ14F40. We are grateful to the study mothers and fathers, the twins, and the twins' teachers for their participation. Our thanks to members of the E-Risk team for their dedication, hard work, and insights.

Word Count: 3,500

Tables: 5

Figures: 0

Abstract

Aims: This study tested whether adolescents who used cannabis or met criteria for cannabis dependence showed neuropsychological impairment prior to cannabis initiation and neuropsychological decline from before to after cannabis initiation.

Design: A longitudinal co-twin control study.

Setting and Participants: Participants were 1,989 twins from the Environmental Risk (E-Risk) Longitudinal Twin Study, a nationally representative birth cohort of twins born in England and Wales from 1994-1995.

Measurements: Frequency of cannabis use and cannabis dependence were assessed at age 18. Intelligence quotient (IQ) was obtained at ages 5, 12, and 18. Executive functions were assessed at age 18.

Findings: Adolescents who used cannabis had lower IQ in childhood, prior to cannabis initiation, and had lower IQ at age 18, but there was little evidence that cannabis use was associated with IQ decline from age 12-18. For example, adolescents with cannabis dependence had age-12 and age-18 IQ scores that were 5.61 ($t=-3.11$, $p=.002$) and 7.34 IQ points ($t=-5.27$, $p<.001$) lower than adolescents without cannabis dependence, but adolescents with cannabis dependence did not show greater IQ decline from age 12-18 ($t=-1.27$, $p=.20$). Moreover, adolescents who used cannabis had poorer executive functions at age 18, but these associations were generally not apparent within twin pairs. For example, twins who used cannabis more frequently than their co-twin performed similarly to their co-twin on 5 of 6 executive function tests ($ps>.10$). The one exception was that twins who used cannabis more frequently than their co-twin performed worse on one working memory test (Spatial Span Reversed; $\beta=-0.07$, $p=.036$).

Conclusions: Family background factors explain why adolescent cannabis users perform worse on IQ and executive function tests. Therefore, short-term cannabis use in adolescence does not appear to cause IQ decline or impair executive functions, even when cannabis use reaches the level of dependence.

Associations between Adolescent Cannabis Use and Neuropsychological Decline:

A Longitudinal Co-Twin Control Study

Debate concerning cannabis legalization has led to increased urgency to understand the effects of cannabis use on health and behavior (1). The effect of cannabis use on neuropsychological functions has received considerable research attention, and the general consensus is that heavy cannabis use is associated with neuropsychological impairment (2-7). However, there is uncertainty regarding the extent to which neuropsychological impairment is apparent prior to cannabis use initiation, the age at which cannabis-related neuropsychological impairment first emerges, and the level and duration of cannabis exposure that is sufficient to produce impairment. One hypothesis is that neuropsychological impairment is apparent in childhood, prior to cannabis use initiation. A second hypothesis is that cannabis-induced neuropsychological impairment first emerges in adolescence shortly after cannabis use initiation. Yet a third hypothesis is that cannabis-induced neuropsychological impairment emerges only after years of heavy use. Determining which hypothesis has more support will have critical implications for prevention and remediation.

To address these questions, prospective longitudinal studies are needed. There are only nine cohort studies of the association between cannabis use and neuropsychological impairment that could inform these questions. These studies included adolescents or young adults in the sample and administered neuropsychological tests at two or more time points (**Supplemental Table 1**). Six of these studies assessed neuropsychological functions in childhood, prior to cannabis use initiation, and therefore had ‘before and after’ assessments of neuropsychological functions (8, 11, 12, 14-17). These six studies found inconsistent evidence for the hypothesis that neuropsychological impairment predates cannabis initiation (8, 11, 12, 14-17).

Across all nine studies, there was mixed evidence that cannabis use was associated with neuropsychological decline (or neuropsychological impairment after accounting for baseline neuropsychological functioning). However, studies varied in terms of length of follow-up and the cohorts' level of cannabis exposure. In general, studies with the longest follow-up (8, 9) and greatest cannabis exposure (8, 9, 11) tended to show the strongest evidence of cannabis-related neuropsychological decline, and studies with the shortest follow-up period and least cannabis exposure (14-17) (i.e., studies of adolescent cannabis use) tended to show the weakest evidence. This pattern is consistent with the hypothesis that cannabis-induced neuropsychological impairment emerges only after years of heavy cannabis use. Nonetheless, firm conclusions cannot be drawn for several reasons. First, there are relatively few cohort studies, particularly studies that assessed neuropsychological functions prior to cannabis initiation. Second, existing cohort studies of adolescents examined low-level cannabis use (14-17), leaving open the possibility that neuropsychological impairment might emerge only for adolescents with more problematic use. Third, there are many potential confounders of cannabis-neuropsychological impairment associations, limiting causal inference.

The purpose of the present study was to test associations between adolescent cannabis use and neuropsychological decline in a cohort of British children followed prospectively from age 5-18. Like the few existing cohort studies of adolescent cannabis use (11, 14-17), we assessed intelligence (IQ) in childhood, prior to cannabis use initiation. We also assessed IQ and executive functions at age 18, after some cohort members had begun using cannabis. Unlike other cohort studies of adolescent cannabis use (11, 14-16), we examined cannabis dependence as our cannabis exposure, in addition to frequency of cannabis use, as cannabis dependence is an indicator of more problematic use. Further, because the cohort comprises twin pairs, it enabled a

comparison of neuropsychological decline for twins in the same family who differed in their cannabis use. This within-pair comparison is important because it controls for family background factors that might lead to a spurious association between cannabis use and neuropsychological decline.

Methods

Participants

Participants were members of the Environmental Risk (E-Risk) Longitudinal Twin Study, which tracks the development of a birth cohort of 2,232 British children. The sample was drawn from a larger birth register of twins born in England and Wales in 1994–1995 (19). Full details about the sample are reported elsewhere (20). Briefly, the E-Risk sample was constructed in 1999–2000, when 1,116 families (93% of those eligible) with same-sex 5-year-old twins participated in home-visit assessments. This sample comprised 56% monozygotic (MZ) and 44% dizygotic (DZ) twin pairs; sex was evenly distributed within zygosity (49% male). Families were recruited to represent the UK population of families with newborns in the 1990s, on the basis of residential location throughout England and Wales and mother's age. Teenaged women with twins were over-selected to replace high-risk families lost to the register through nonresponse. Older women having twins via assisted reproduction were under-selected to avoid an excess of well-educated older women. These strategies ensured that the study sample represents the full range of socioeconomic conditions in Great Britain, as reflected in the families' distribution on a neighborhood-level socioeconomic index (ACORN [A Classification of Residential Neighborhoods], developed by CACI Inc. for commercial use) (21, 22): 25.6% of E-Risk families live in “wealthy achiever” neighborhoods compared with 25.3% nationwide; 5.3% vs. 11.6% live in “urban prosperity” neighborhoods; 29.6% vs. 26.9% live in “comfortably off”

neighborhoods; 13.4% vs. 13.9% live in “moderate means” neighborhoods; and 26.1% vs. 20.7% live in “hard-pressed” neighborhoods. E-Risk underrepresents “Urban Prosperity” because such households are significantly more likely to be childless.

Follow-up home visits were conducted when the children were aged 7 (98% participation), 10 (96% participation), 12 (96% participation), and 18 years (93% participation). Home visits at ages 5, 7, 10, and 12 included assessments with participants and their mothers; we conducted interviews only with participants at age 18 (n=2066). There were no differences between those who did and did not take part in the study at age 18 in terms of key measures when the cohort was initially defined at age 5: socioeconomic status ($\chi^2=0.86$, $p=.65$), IQ ($t=0.98$, $p=.33$), or internalizing or externalizing problems ($t=0.40$, $p=.69$ and $t=0.41$, $p=.68$, respectively). Here we report on n=1,989 individuals with IQ data at ages 5, 12, and 18, which comprised 96% of all participants seen at age 18. Sample characteristics are shown in **Table 1**.

The Joint South London and Maudsley and the Institute of Psychiatry Research Ethics Committee approved each phase of the study. Parents gave written informed consent and twins gave assent between ages 5-12 and written informed consent at age 18.

Measures

Cannabis Use

Participants were evaluated for past-year cannabis dependence at age 18 according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria (23). Four percent (n=84) of participants were diagnosed with cannabis dependence. Of the 977 complete twin pairs, most were concordant for not having cannabis dependence (n=908 pairs). Twelve pairs were concordant for dependence and 57 pairs were discordant for cannabis dependence.

Participants reported on how often they used cannabis in the past year at age 18. Responses were: ‘0’=never (63%), ‘1’=less than monthly (28%), ‘2’=monthly (3%), ‘3’=weekly (3%), ‘4’=daily (2%), and ‘5’=many times a day (1%). The correlation between twins within a pair on frequency of use was $r=0.55$ ($p<.001$).

Intelligence Quotient (IQ)

Intelligence was assessed at ages 5 and 12, before cannabis initiation, and again at age 18. (Only 19 participants had tried cannabis at age 12.) At age 5, we used a short form of the Wechsler Preschool and Primary Scale of Intelligence-Revised (WPPSI-R) (24). Using two subtests (Vocabulary and Block Design), we pro-rated children’s age-5 IQ following procedures described by Sattler (25). At age 12, we used the Wechsler Intelligence Scale for Children-Revised (WISC-R) (26). At age 18, we used the Wechsler Adult Intelligence Scale–IV (WAIS-IV) (27). At ages 12 and 18, two of the same subtests were administered -- Information and Matrix Reasoning. These two subtests were used to obtain pro-rated full-scale IQ at ages 12 and 18. Pro-rated full-scale IQ scores were standardized on the full sample at each age to $M=100$, $SD=15$, and subtest scores were standardized to $M=10$, $SD=3$.

Executive Functions

At age 18, executive functions tapping attention/vigilance and working memory were assessed with tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (28). The CANTAB is a computerized test battery of neuropsychological functioning that uses touch-screen technology. Tests are described in **Supplemental Table 2**. Scores on each executive function test were standardized to $M=0$, $SD=1$.

Statistical Analyses

We used linear regression to test whether age-18 cannabis use was associated with (a) lower IQ at ages 5, 12, and 18, (b) IQ decline from age 12-18 (with IQ decline represented as a change score: age-18 IQ minus age-12 IQ), and (c) poorer executive functioning at age 18. We focused on IQ decline from age 12-18 (and not age 5-18) because the age-12 and age-18 IQ scores were based on the same two subtests (Information and Matrix Reasoning) whereas the age-5 IQ scores were based on different subtests. However, age-5 IQ was included as a covariate in analyses of IQ decline. For tests of associations between cannabis use and executive functioning at age 18, we included age-12 IQ as a covariate. Sex was included as a covariate in all analyses, as, relative to girls, boys had higher rates of cannabis use and dependence, had slightly higher IQ at ages 12 and 18, and showed a greater increase in IQ from age 12-18 (**Table 1**). However, there was little evidence that associations between cannabis use and neuropsychological functioning differed for boys and girls.

We conducted analyses in the full sample of twins, which approximates the general population, and adjusted for the non-independence of observations (twins nested within twin pairs) by using the SURVEYREG procedure in SAS. The SURVEYREG procedure uses Taylor linearization to estimate sampling errors of estimators. We also conducted co-twin control analyses comparing twins within the same family who differed in their level of cannabis use. Co-twin control analyses allow us to come closer to causal inference because they inherently control for a variety of unmeasured family background factors. The logic is as follows. In the full sample of twins, differences between cannabis dependent and non-dependent adolescents, for example in terms of SES, neighborhood, or educational opportunities, could lead to a spurious association between cannabis dependence and lower IQ. In contrast, twins from the same family share

family backgrounds, and therefore, these family factors cannot explain IQ differences between twins discordant for dependence.

Co-twin control analyses differed slightly depending on the cannabis exposure. For cannabis dependence, analyses were conducted as described above for the full sample, but the sample was limited to the 57 twin pairs discordant for dependence. For frequency of cannabis use, we used all complete twin pairs ($n=977$) and computed twin difference scores for frequency of use (e.g., twin-1 frequency minus twin-2 frequency) and outcomes (IQ at ages 5, 12, and 18; IQ decline from 12-18; and age-18 executive functions). Then, we regressed twin differences in outcomes on twin differences in frequency of use. Findings from co-twin control analyses are reported for the combined sample of DZ and MZ twins to avoid loss of power resulting from reporting on them separately. There was little evidence that associations differed by zygosity.

Results

Associations between Cannabis Dependence and IQ

Table 2 shows mean pro-rated IQ scores for cannabis-dependent and non-dependent adolescents in the full sample and in the subsample of discordant twin pairs. First, we review findings for the full sample. Adolescents with cannabis dependence at age 18 had lower IQ at ages 5, 12, and 18 (95.18, 94.95, and 93.14, respectively) compared with non-dependent adolescents (100.48, 100.56, and 100.48, respectively), but there was only weak evidence that adolescents with cannabis dependence showed greater IQ decline from age 12-18 (-1.81 IQ points) than non-dependent adolescents (-0.08 IQ points) ($t=-1.27$, $p=.20$) (**Table 2**). Findings were similar after controlling for age-5 IQ.

Results for discordant twin pairs differed from results for the full sample in that twins with cannabis dependence performed similarly to their co-twins without cannabis dependence on

the IQ tests at each age (**Table 2**). For example, cannabis-dependent twins had an age-5 IQ of 94.26, and their non-dependent co-twins had an age-5 IQ of 93.50 (**Table 2**). Thus, the average age-5 IQ difference between discordant twins was only 0.76 IQ points. (This same result is obtained by subtracting twin-1 IQ from twin-2 IQ within a discordant pair and averaging that difference across twins.) Therefore, unlike in the full sample, there was no evidence from discordant pairs that cannabis-dependent adolescents had lower IQ at any age, suggesting that family background factors explain why, in the full sample, cannabis-dependent adolescents had lower IQ. That family factors confounded the cannabis-IQ association is also apparent in the means for discordant twin pairs, which show that both the cannabis-dependent and non-dependent twins from discordant pairs had lower IQ relative to the full sample. That is, non-dependent adolescents from families in which a sibling had dependence had lower IQ relative to norms (mean IQ=100).

Findings for the full sample and the subsample of discordant twins were similar after excluding 19 participants who had used cannabis at age 12 (**Supplemental Table 3**). Results for the Information and Matrix Reasoning subtests were similar to results for full-scale IQ (**Supplemental Tables 4-5**).

Associations between Frequency of Cannabis Use and IQ

Because only 4% of twins were cannabis dependent but 37% of them had used cannabis, we repeated all analyses based on frequency of cannabis use. This allowed for greater variation and power to detect differences. In the full sample, more frequent cannabis use at age 18 was associated with lower IQ at ages 12 and 18 (but not age 5) and greater IQ decline from age 12-18, but the effect was small (**Table 3**). For every standard deviation increase in frequency of cannabis use, IQ declined by an additional 0.05 standard deviations. Associations were similar

after controlling for age-5 IQ. Among twin pairs, we found that the more frequently cannabis-using twin did not show lower IQ at any age or greater IQ decline than their co-twin (**Table 3**).

We conducted sensitivity analyses comparing IQ for adolescents who did not use cannabis at age 18 with adolescents who used cannabis at least weekly, under the hypothesis that relatively trivial differences between adolescents in frequency of use obscure effects at the extremes of use. However, there was little evidence that weekly cannabis users showed greater IQ decline than non-users (**Supplemental Table 6**).

Associations between Cannabis Dependence and Executive Functions

Table 4 shows mean executive function scores at age 18 for cannabis-dependent and non-dependent adolescents in the full sample and in the subsample of discordant twins. In the full sample, cannabis-dependent adolescents performed worse on 4 of 6 tests (RVP A Prime, SWM Strategy, Spatial Span Forward, and Spatial Span Reversed). After controlling for age-12 IQ, cannabis-dependent adolescents performed worse on only 2 of 6 tests (Spatial Span Forward and Reversed). However, no differences were apparent among discordant twins.

Associations between Frequency of Cannabis Use and Executive Functions

In the full sample, more frequent cannabis use at age 18 was associated with worse performance on all executive function tests except one, even after controlling for age-12 IQ (**Table 5**). However, most of these associations were not apparent within twin pairs – i.e., when we compared each twin to their co-twin. (**Table 5**). The only exception was that twins who used cannabis more frequently than their co-twin performed worse on the Spatial Span Reversed task, but the effect was small ($\beta=-0.07$, $p=.022$).

We conducted sensitivity analyses comparing adolescents who had not used cannabis in the past year with adolescents who had used cannabis at least weekly in the past year (**Supplemental Table 7**). Findings were similar.

Discussion

In a cohort of British youth followed from age 5-18, we found that youth who used cannabis at age 18 had lower IQ in childhood, prior to cannabis initiation, and had lower IQ at age 18, but there was little evidence that cannabis use was associated with IQ decline from age 12-18. Moreover, although cannabis use was associated with lower IQ and poorer executive functions at age 18, these associations were generally not apparent within pairs of twins from the same family, suggesting that family background factors explain why adolescents who use cannabis perform worse on IQ and executive function tests. Results were similar regardless of how we defined cannabis exposure – i.e., in terms of frequency of use or the more problematic outcome of dependence. Findings suggest that cannabis use does not cause IQ decline or impair executive functions in adolescence after relatively short-term use, even when use reaches the level of dependence.

Our finding that lower IQ predates cannabis use contributes to already mixed findings in this area. Of the six cohort studies that obtained neuropsychological data prior to cannabis use initiation, four found no evidence that lower IQ predated cannabis use (8, 12, 15, 17), and two found at least some evidence that lower IQ or poorer executive functions predated cannabis use (14, 16) (**Supplemental Table 1**). The reasons for this discrepancy are unclear. One potential explanation is that birth-cohort differences in structural factors (e.g., cannabis price, ease of access to cannabis) explain between-study differences in adolescent characteristics (e.g., socioeconomic status, IQ) associated with cannabis use.

We found that adolescents with cannabis dependence showed similar changes in IQ from age 12-18 to adolescents without cannabis dependence. This lack of an association between cannabis dependence and IQ decline was apparent in the full sample of twins, a sample that approximates the general population, and in the subsample of twins discordant for cannabis dependence. Results were generally similar when we considered frequency of cannabis use as our exposure, with one exception. There was some evidence that more frequent cannabis use (considered on a continuum from no use to many uses per day) was associated with IQ decline in the full sample, but the effect size was small. Further, this association was not apparent within twin pairs in an analysis that inherently controlled for family background factors. Overall, there was limited evidence that cannabis use was associated with IQ decline during adolescence.

Our finding that adolescent cannabis use was not associated with IQ decline is broadly consistent with findings from several recent cohort studies (14-17), one of which used a co-twin control design (14), similar to the current study. Our study builds on these previous studies by showing no effect of a more problematic level of cannabis use -- cannabis dependence. Notably, accumulating findings of no association between cannabis use and IQ decline in adolescence do not conflict with our previous report from the Dunedin Study that persistent cannabis use is associated with IQ decline. In that study, adolescents who met criteria for cannabis dependence persistently through adulthood showed an 8-point IQ decline from age 18-38, whereas adolescents who met criteria for cannabis dependence only at age 18 (and not thereafter) did not show IQ decline (8), similar to what we report here.

In the current study, adolescent cannabis use was associated with impaired executive functions, including impaired attention/vigilance and spatial working memory, in the full sample but not in the subsample of twin pairs. For example, twins with cannabis dependence performed

no worse on executive function tests than their co-twins without cannabis dependence, suggesting that family background factors contribute to a spurious association between cannabis dependence and impaired executive functions in the general population. However, when we used frequency of cannabis use as our exposure, we found that more frequently cannabis using twins performed slightly worse on the Spatial Span Reversed test than their co-twins who used cannabis less frequently, suggesting a possible causal association between cannabis use and impairment on this one test. However, this finding might have been a false positive, particularly given previous inconsistent findings of an association between cannabis use and working memory (5).

This study has limitations. First, cannabis use was based on self-reports. Although this is typical for cohort studies, biological tests could have helped to detect under-reporting. Second, although we tested associations between cannabis use and multiple executive function tests, we lacked tests of other neuropsychological functions, such as memory, which has been shown to be impaired in adolescent cannabis users (7, 29). Third, due to small sample sizes, discordant twin analyses may have been underpowered to detect effects. We note, however, that effect sizes were close to zero in many analyses. Fourth, although we were able to examine cannabis dependence, a level of problem use that has not been studied in previous cohorts of adolescents, it is possible that cannabis-related neuropsychological impairment only becomes apparent after more intense cannabis use (e.g., multiple uses per day), which was rare in our cohort at 1% prevalence. Very large cohort studies, like the Adolescent Brain Cognitive Development study of 10,000 9-10 years followed for 10 years (30), are needed to obtain a sufficient number of adolescents from the general population who use cannabis intensely.

This study has a number of implications. First, to accurately interpret associations between cannabis use and neuropsychological impairment, it is important to test neuropsychological functions before cannabis initiation. Second, relatively short-term cannabis use in adolescence does not appear to cause IQ decline or impair executive functions, even when cannabis use reaches the level of dependence. Third, more research is needed to test the possibility that cannabis-related neuropsychological impairment develops gradually over time such that obvious impairment is only apparent in older, longer-term persistent users.

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Table 1. Sample characteristics.

Characteristic	Full Sample (N=1989)	Girls (N=1049)	Boys (N=940)	Test of Sex Difference	
	M (SD)	M (SD)	M (SD)	β /OR	p
Sex (% Male)	47.26	-	-	-	-
Zygosity (% Dizygotic)	43.99	42.70	45.42	OR=1.12 ^a	.39
SES	2.00 (0.82)	2.01 (0.82)	1.99 (0.81)	-0.01	.79
Age 5 IQ	100.19 (15.00)	100.21 (14.37)	100.17 (15.69)	0.00	.97
Age 12 IQ	100.33 (14.75)	99.31 (13.64)	101.47 (15.83)	0.07	.012
Age 18 IQ	100.17 (14.88)	98.27 (13.95)	102.30 (15.59)	0.14	<.001
Cannabis Use (% Used in Past Year)	37.56	30.03	45.96	OR=1.98 ^a	<.001
Cannabis Dependence (%)	4.22	2.57	6.06	OR=2.44 ^a	<.001

Note. SES=socioeconomic status. SES was assessed on a three-point scale with 1=low SES and 3=high SES. a. These analyses used logistic regression to test whether boys had greater odds of being a dizygotic (versus monozygotic) twin than girls; greater odds of past-year cannabis use; and greater odds of cannabis dependence than girls. All other analyses used linear regression (i.e., to test whether boys had higher SES and higher IQ than girls), and standardized beta coefficients are reported.

Table 2. Mean pro-rated IQ scores at ages 5, 12, and 18 and average within-person IQ change from age 12 to 18 as a function of cannabis dependence at age 18.

	Non-Dependent Adolescents (N=1905)	Cannabis Dependent Adolescents (N=84)	Difference Between Non-Dependent and Cannabis Dependent Adolescents ^a			Difference Between Non-Dependent and Cannabis Dependent Adolescents After Controlling for Age 5 IQ ^a		
				t	p		t	p
Full sample								
Age 5 IQ	100.41	95.18	-5.23	-2.94	.003	-	-	-
Age 12 IQ	100.56	94.95	-5.61	-3.11	.002	-2.80	-1.78	.08
Age 18 IQ	100.48	93.14	-7.34	-5.27	<.001	-4.82	-3.88	<.001
IQ Change From Age 12-18 ^b	-0.08	-1.81	-1.73	-1.27	.20	-2.02	-1.49	.14
Discordant Twins	Non-Dependent Twins (N=57)	Cannabis Dependent Co-Twin (N=57)	Difference Between Discordant Twin Pairs ^a			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a		
				t	p		t	p
Age 5 IQ	93.50	94.26	0.76	0.39	.70	-	-	-
Age 12 IQ	95.47	93.97	-1.50	-0.80	.43	-1.81	-0.94	.35
Age 18 IQ	94.31	92.86	-1.45	-0.81	.42	-1.77	-0.97	.33
IQ Change From Age 12-18 ^b	-1.16	-1.11	0.05	0.02	.98	0.04	0.02	.99

Note. Means and statistical tests are adjusted for sex. a. Negative scores indicate that adolescents with cannabis dependence showed lower IQ/greater IQ decline than non-dependent adolescents. For example, results for the full sample show that IQ decline for adolescents with cannabis dependence was 1.73 points greater than IQ decline for adolescents without cannabis dependence. b. IQ change was represented as a change score (age 18 IQ – age 12 IQ). We focused on IQ decline from age 12 to 18 because the age 12 and age 18 pro-rated IQ scores were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 pro-rated IQ scores were based on different subtests (Vocabulary and Block Design). Results are shown with and without adjustment for age 5 IQ. Statistically significant differences are shown in bold.

Table 3. Associations between frequency of cannabis use at age 18 and (a) pro-rated IQ at ages 5, 12, and 18, and (b) IQ decline from age 12 to 18.

	Before Controlling for Age 5 IQ		After Controlling for Age 5 IQ	
Full Sample (n=1,989)	β^a	p	β^a	p
Age 5 IQ	-0.05	.07	-	-
Age 12 IQ	-0.11	<.001	-0.08	<.001
Age 18 IQ	-0.15	<.001	-0.12	<.001
IQ Change from Age 12-18 ^c	-0.05	.035	-0.05	.023
Twin Pairs (n=977 twin pairs)	β^b	p	β^b	p
Age 5 IQ	0.02	.56	-	-
Age 12 IQ	0.03	.32	0.03	.37
Age 18 IQ	0.00	.94	0.00	.97
IQ Change from Age 12-18 ^c	-0.02	.46	-0.02	.47

Note. Estimates are standardized regression coefficients. All associations are adjusted for sex. a. Negative estimates indicate that more frequent cannabis use at age 18 was associated lower IQ/greater IQ decline from age 12 to 18. b. Positive estimates indicate that the twin who used cannabis more frequently at age 18 showed higher IQ/less IQ decline than their co-twin. c. IQ change was represented as a change score (age 18 IQ – age 12 IQ). We focused on IQ decline from age 12 to 18 because the age 12 and age 18 pro-rated IQ scores were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 pro-rated IQ scores were based on different subtests (Vocabulary and Block Design). Results are shown with and without adjustment for age 5 IQ. Statistically significant differences are shown in bold.

Table 4. Mean executive function scores at age 18 as a function of cannabis dependence at age 18.

Executive Function Test	Full Sample								Discordant Twins							
	Before Controlling for Age 12 IQ				After Controlling for Age 12 IQ				Before Controlling for Age 12 IQ				After Controlling for Age 12 IQ			
	Not Dep (N= 1,902)	Dep (N= 84)	t	p	Not Dep (N= 1,902)	Dep (N= 84)	t	P	Not Dep (N= 57)	Dep (N= 57)	t	p	Not Dep (N= 57)	Dep (N= 57)	t	p
RVP A Prime	0.02	-0.22	-2.26	.024	0.01	-0.07	-0.85	.39	-0.12	-0.21	-0.65	.52	-0.13	-0.20	-0.49	.62
RVP Total False Alarms ^a	0.00	0.02	0.21	.83	0.00	-0.06	-0.57	.57	0.30	0.07	-1.11	.27	0.32	0.06	-1.23	.22
SWM Total Errors ^a	-0.01	0.18	1.80	.07	-0.01	0.04	0.54	.59	0.25	0.15	-0.69	.49	0.27	0.13	-0.97	.34
SWM Strategy ^a	-0.01	0.21	2.40	.017	0.00	0.08	1.00	.32	0.24	0.19	-0.36	.72	0.26	0.17	-0.62	.54
Spatial Span Forward	0.02	-0.48	-4.57	<.001	0.01	-0.35	-3.60	<.001	-0.18	-0.38	-1.30	.20	-0.19	-0.37	-1.15	.26
Spatial Span Reversed	0.01	-0.33	-3.37	<.001	0.01	-0.20	-2.17	.030	-0.16	-0.26	-0.75	.46	-0.17	-0.25	-0.59	.56

Note. Means and statistical tests are adjusted for sex. a. Higher scores are worse. Not dep=not cannabis dependent. Dep=cannabis dependent. RVP=Rapid Visual Processing. SWM=Spatial Working Memory. For the full sample, Ns ranged from 1895 to 1902 for the non-dependent group and 83-84 for the dependent group, as a few people from each group did not complete all executive function tests. For discordant twins, Ns ranged from 56 to 57 twin pairs. Statistically significant differences are shown in bold.

Table 5. Associations between frequency of cannabis use at age 18 and performance on executive function tests at age 18.

Executive Function Test	Full Sample (n=1985)				Twin Pairs (n=974 pairs)			
	Before Controlling for Age 12 IQ		After Controlling for Age 12 IQ		Before Controlling for Age 12 IQ		After Controlling for Age 12 IQ	
	β	p	β	p	β	p	β	p
RVP A Prime	-0.10	<.001	-0.05	.020	0.00	.96	-0.01	.76
RVP Total False Alarms ^a	0.04	.08	0.01	.56	-0.01	.77	-0.01	.84
SWM Total Errors ^a	0.10	<.001	0.06	.005	0.03	.40	0.03	.29
SWM Strategy ^a	0.10	<.001	.06	<.001	0.01	.87	0.01	.75
Spatial Span Forward	-0.13	<.001	-0.09	<.001	-0.04	.22	-0.05	.14
Spatial Span Reversed	-0.13	<.001	-0.09	<.001	-0.07	.036	-0.07	.022

Note. Ns for the full sample ranged from 1978-1985. Ns for twin pairs ranged from 967-974 twin pairs. Ns varied slightly as not all adolescents completed each executive function test. Estimates are standardized beta coefficients, adjusted for sex. RVP=Rapid Visual Processing. SWM=Spatial Working Memory. a. Higher scores are worse, so on these tests, positive coefficients for the full sample indicate that more frequent cannabis use was associated with worse performance on executive functions tests, and positive coefficients for twin pairs indicate that the twin who used cannabis more frequently performed worse on the executive function test than their co-twin. For all other tests, lower scores are worse, so negative coefficients indicate that more frequent cannabis use was associated with worse test performance. Statistically significant associations are shown in bold.

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
Meier et al. 2012 (8)	874	25 y	7-13	38	28% never used cannabis; 58% used cannabis but never regularly (at least 4 days per week); 5% used regularly at one point in their lives; 9% were persistent regular users (used regularly at two or more points in their lives). Of those who had used cannabis, 55% never diagnosed with cannabis dependence; 9% diagnosed at one point in their lives; and 8% diagnosed	Partially	IQ, executive functions, memory, processing speed, perceptual reasoning, verbal comprehension	There was no evidence that neuropsychological impairment was apparent prior to cannabis use initiation.	Persistent cannabis use from age 18-38 was associated with IQ decline from age 7-13 to age 38, even after accounting for a variety of covariates. Persistent cannabis use from age 18-38 was also associated with poorer executive functions, memory, processing speed, perceptual reasoning, and verbal comprehension at age 38, even after accounting for age 7-13 IQ.

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Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
					with cannabis dependence persistently.				
Auer et al. 2016 (9)	3,385	25 y	18-30	43-55	16% never used cannabis; 44% had used cannabis daily for <0.5 years; 24% had used cannabis daily for 0.5-2 years; 7% had used cannabis daily for 2-5 years; 9% had used cannabis daily for >5 years.	No	Verbal memory, processing speed, executive functions	This study could not test whether neuropsychological impairment was apparent prior to cannabis use, as participants had already initiated cannabis use at the time of the first neuropsychological assessment.	Cumulative lifetime cannabis use was associated with worse verbal memory, processing speed, and executive function in adulthood. After accounting for earlier cognitive functioning and a variety of covariates, cumulative cannabis use was associated with worse verbal memory in adulthood.
Lyketsos et al. 1999 (10)	1,318	12 y	18-64	30-76	61% had never used cannabis (non-users); 28% had used cannabis but never used it daily or more often for over 2 weeks (light	Yes	Mini-Mental Status Exam	This study could not test whether neuropsychological impairment was apparent prior to cannabis use, as participants had already initiated cannabis use at the time of the first	Light and heavy cannabis users did not show greater decline on the mini-mental status exam than non-users.

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Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
					users); 11% had used cannabis daily or more often for over 2 weeks (heavy users).			neuropsychological assessment.	
Fried et al. 2005 (11)	113	~8 y	9-12	17-21	52% of the sample had never used cannabis; 17% of the sample were current light users (<5 joints per week) and had consumed a total of M=122 joints; 17% of the sample were current heavy users (>5 joints per week) and had consumed a total of M=1884	Partially	IQ, processing speed, vocabulary, immediate and delayed memory, working memory, sustained attention, abstract reasoning	This study did not report on whether neuropsychological impairment was apparent prior to cannabis use initiation, although a prior report based on this cohort found no evidence that cannabis users had lower IQ prior to cannabis use initiation (12).	Current heavy cannabis users performed worse than non-users on IQ, processing speed, and immediate and delayed memory in young adulthood, even after accounting for pre-drug performance on the relevant cognitive test and a variety of covariates. Current light users and former cannabis users did not perform worse than non-users on any test.

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
					joints; and 14% were former users (no regular use for 3+ months and <3 joints in the past 2 months at the age 17-21 assessment) and had consumed a total of M=2203 joints.				
Tait et al. 2011 (13)	1,499	8 y	20-24	28-32	28% of the sample had never used; 44% were classified as always former users (had used cannabis prior to baseline but not thereafter); 15% were classified as	Yes	Immediate and delayed recall, short-term memory, verbal ability, processing speed	This study could not test whether neuropsychological impairment was apparent prior to cannabis use, as participants had already initiated cannabis use at the time of the first neuropsychological assessment.	Analyses compared change in neuropsychological functions for the following groups: former heavy cannabis users vs. remain heavy cannabis users; former light users vs. remain light users; never users vs. former heavy users; never users vs. former light users; and never users versus always former users. After adjustment for covariates, the only statistically significant findings were as

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
					former light (monthly or less) users (light use prior to the last wave of data collection and no use at the last wave); 4% were classified as former heavy (at least weekly) users; 5% were classified as remain light users; and 4% were classified as remain heavy users.				follows: Former heavy cannabis users showed improvement in immediate recall relative to heavy users.
Jackson et al. 2016 (14)	Sample 1: 789; Sample 2: 2,277	10 y; ~7 y	Sample 1: 9-10; Sample 2: 11-12	Sample 1: 19-20; Sample 2: 17-19	Sample 1: 60% of the sample had used cannabis; 30% had used cannabis 30+ times; 12.5% had used cannabis daily	Yes	IQ	There was mixed evidence that cannabis users had lower IQ prior to cannabis use initiation.	Cannabis use (defined as ever use) was associated with decline in Vocabulary and Information subtests, even after accounting for a variety of sociodemographic covariates. Associations were no longer apparent in sample 2 after accounting for other substance

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
					for 6-12 months; Sample 2: 36% of the sample had used cannabis; 13% had used cannabis 30+ times; 8% had used cannabis daily for 6-12 months.				use. There was no evidence that cannabis use was associated with decline in Similarities, Block Design, Matrix Reasoning, and Picture Arrangement subtests. Use of cannabis 30+ times and daily cannabis use for 6-12 months were also not associated with IQ decline among users. Moreover, among twins discordant for cannabis use, cannabis use was not associated with IQ decline on any subtest.
Mokrysz et al. 2016 (15)	2,235	7 y	8	15	77% had never used cannabis; 11% had used cannabis <5 times; 6% had used cannabis 5-19 times; 3% has used cannabis 20-49 times; 3% had used cannabis 50+ times.	No	IQ	There was no evidence that cannabis users had lower IQ prior to cannabis use initiation.	Cumulative cannabis use by age 15 was associated with lower IQ at age 15, after controlling for age 8 IQ. This association was no longer apparent after controlling for covariates.

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
Castellanos-Ryan et al. 2016 (16)	294	7 y	13	20	Average cannabis use ranged from no use in the past year at age 14 to between 3-5 and 6-9 uses in the past year at age 17.	Partially	Verbal IQ, short-term memory, executive functions	Higher verbal IQ at age 13 was associated with an earlier age of onset of cannabis use and greater increases in frequency of cannabis use from ages 14-17. Poorer short-term memory and working memory at age 14 were associated with an earlier age of onset of cannabis use.	Greater frequency of cannabis use at age 14 was associated with decline in one of several tests of executive functions, even after controlling for a variety of covariates. Greater increases in cannabis use from age 14-17 were associated with decline in verbal IQ and one of several tests of executive functions, with the association with verbal IQ becoming non-significant after controlling for covariates.
Boccio & Beaver, 2017 (17)	Varied from 373 to 6,584	6 y	12-21 (Wave I)	18-26 (Wave III)	No participants had used cannabis at Wave I. 12% had used cannabis in the past year at Wave II and 70% had used cannabis in the past year at Wave III. Among cannabis	Yes	Verbal IQ	There was no evidence that cannabis users had lower IQ prior to initiation.	Dichotomous measures of cannabis use (e.g. past-year cannabis use vs. no use) at Waves II and III were each associated with verbal IQ decline from Waves I-III. However, number of cannabis use days in the past month at Waves II and III were not associated with verbal IQ decline from Waves I-III. There was also inconsistent evidence of cannabis-related verbal IQ decline based on cannabis use

Supplemental Table 1. Cohort studies of associations between cannabis use and neuropsychological functioning. Studies are organized by length of follow-up and date.

Study	Sample Size	Length of Follow-Up	Baseline Age or Age Range	Follow-Up Age or Age Range	Level of Cannabis Exposure	Same Tests Across Time?	Neuropsychological Domains	Findings: Neuropsychological Differences Before Cannabis Initiation	Findings: Cannabis-Related Change in Neuropsychological Function
					users, the average number of days of cannabis use in the past-month at Waves II and III was 3 and 7 days, respectively.				data combined across Waves II and III.

Note. This table includes only those cohort studies with (a) adolescents or young-adults in the sample, (b) neuropsychological testing at two or more time points, and (c) follow-up of at least 1 year. There was one longitudinal case-control study of adolescents with and without a diagnosis of substance use disorder, and it found that cumulative cannabis use from ~ age 16 to 24 was associated with poorer attention in young adulthood, even after controlling for baseline attention and other covariates. However, cannabis use was not associated with poorer neuropsychological function in other domains (language, visuospatial abilities, verbal learning and memory, and executive functions) (18).

Supplemental Table 2. Description of executive function measures from the Cambridge Neuropsychological Test Automated Battery (CANTAB).

Test	Description
Rapid Visual Information Processing (RVP)	This is a test of sustained attention and vigilance. A white box appears in the center of the computer screen, inside which digits from 2 to 9 appear in a pseudo-random order at the rate of 100 digits per minute. Subjects are requested to detect target sequences of digits (for example, 2-4-6, 3-5-7, 4-6-8) and to register responses using the press pad. At the most difficult level, the participant scans simultaneously for two target sequences.
RVP A-prime	This is a signal detection measure of sensitivity to the target, regardless of response tendency (range 0.00 to 1.00; bad to good) and is a measure of how good the subject is at detecting target sequences using "Probability of Hit" and "Probability of False Alarm." Higher scores are better.
RVP Total False Alarms	This measure records impulsive jumping to respond too soon before the correct target digit sequence is complete. Because relatively few participants made numerous false alarms, this measure is categorical, coded 0=none, 1=1 false alarm, 2=2 or more false alarms. Higher scores are worse.
Spatial Working Memory Test	The test begins with a number of colored squares (boxes) being shown on the screen. The aim of this test is that, by touching the boxes and using a process of elimination, the participant should find one blue 'token' in each of a number of boxes and use them to fill up an empty column on the right hand side of the screen. The number of boxes is gradually increased, until it is necessary to search a total of eight boxes. The color and position of the boxes used are changed from trial to trial to discourage the use of stereotyped search strategies.
Spatial Working Memory Total Errors	This measures assesses capacity to hold information about spatial location in active memory while searching for information. At the most difficult level, participants memorize 10 locations in one problem. Higher scores are worse.

Spatial Working Memory Strategy	This measure records trials on which the participant applied a problem-solving strategy by opening boxes in a systematic sequence. Higher scores are worse (more non-strategic trials).
Spatial Span	This measure is the visual non-verbal equivalent of the oral-auditory Digit Span test and measures working memory. At the most difficult level, participants memorize a sequence of 9 colored stimuli.
Spatial Span Forward	This measure is the visual non-verbal equivalent of the oral-auditory Digit Span forward test. Higher scores are better.
Spatial Span Reversed	This measure is the visual non-verbal equivalent of the oral-auditory Digit Span backward test. Higher scores are better.

Supplemental Table 3. Mean pro-rated IQ scores at ages 5, 12, and 18 and average within-person IQ change from age 12 to 18 as a function of cannabis dependence at age 18. These analyses exclude the 19 participants who had used cannabis at age 12.

	Non-Dependent Adolescents (N=1889)	Cannabis Dependent Adolescents (N=81)	Difference Between Non-Dependent and Cannabis Dependent Adolescents ^a	t	p	Difference Between Non-Dependent and Cannabis Dependent Adolescents After Controlling for Age 5 IQ ^a	t	p
Full sample								
Age 5 IQ	100.40	95.25	-5.15	-2.80	.005	-	-	-
Age 12 IQ	100.61	95.20	-5.41	-2.94	.003	-2.66	-1.66	.10
Age 18 IQ	100.53	93.57	-6.96	-4.95	<.001	-4.86	-3.58	<.001
IQ Change From Age 12-18 ^b	-0.08	-1.63	-1.55	-1.11	.27	-1.83	-1.31	.19
	Non-Dependent Twins (N=54)	Cannabis Dependent Co-Twin (N=54)	Difference Between Discordant Twin Pairs ^a	t	p	Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a	t	p
Discordant Twins								
Age 5 IQ	93.76	94.28	0.52	0.25	.80	-	-	-
Age 12 IQ	95.26	94.24	-1.02	-0.55	.58	-1.23	-0.64	.52
Age 18 IQ	94.58	93.39	-1.19	-0.64	.52	-1.40	-0.79	.45
IQ Change From Age 12-18 ^b	-0.68	-0.85	-0.17	-0.08	.94	-0.18	-0.08	.94

Note. Means and statistical tests are adjusted for sex. a. Negative scores indicate that adolescents with cannabis dependence showed lower IQ/greater IQ decline than non-dependent adolescents. For example, results for the full sample show that IQ decline for adolescents with cannabis dependence was 1.55 points greater than IQ decline for adolescents without cannabis dependence. b. IQ change was represented as a change score (age 18 IQ – age 12 IQ). We focused on IQ decline from age 12 to 18 because the age 12 and age 18 pro-rated IQ scores were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 pro-rated IQ scores were based on different subtests (Vocabulary and Block Design). Results are shown with and without adjustment for age 5 IQ. Statistically significant differences are shown in bold.

Supplemental Table 4. Mean Information subtest scores at ages 12 and 18 and average within-person subtest score change from age 12 to 18 as a function of cannabis dependence at age 18.

	Non-Dependent Adolescents (N=1905)	Cannabis Dependent Adolescents (N=84)	Difference Between Non- Dependent and Cannabis Dependent Adolescents ^a	t	p	Difference Between Non-Dependent and Cannabis Dependent Adolescents After Controlling for Age 5 IQ ^a	t	p
Full sample								
Age 12 Information Subtest	10.10	9.01	-1.09	-2.91	.004	-0.54	-1.70	.09
Age 18 Information Subtest	10.10	8.55	-1.55	-5.58	<.001	-1.04	-4.11	<.001
Change in Subtest Score ^b	0.00	-0.46	-0.46	-1.49	.14	-0.49	-1.64	.10
	Non-Dependent Twins (N=57)	Cannabis Dependent Co-Twin (N=57)	Difference Between Discordant Twin Pairs ^a	t	p	Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a	t	p
Discordant Twins								
Age 12 Information Subtest	8.99	8.94	-0.05	-0.14	.89	-0.11	-0.31	.76
Age 18 Information Subtest	9.12	8.77	-0.35	-1.21	.23	-0.40	-1.35	.18
Change in Subtest Score ^b	0.13	-0.17	-0.30	-0.88	.38	-0.29	-0.82	.41

Note. Means and statistical tests are adjusted for sex. a. Negative scores indicate that adolescents with cannabis dependence showed lower IQ/greater IQ decline than non-dependent adolescents. b. Change in the Information subtest score was represented as a change score (age 18 Information – age 12 Information). We focused on subtest decline from age 12 to 18 because the age 12 and age 18 IQ tests were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 IQ test was based on different subtests (Vocabulary and Block Design). Results are shown with and without adjustment for age 5 IQ. Statistically significant differences are shown in bold.

Supplemental Table 5. Mean Matrix Reasoning subtest scores at ages 12 and 18 and average within-person subtest score change from age 12 to 18 as a function of cannabis dependence at age 18.

	Non-Dependent Adolescents (N=1905)	Cannabis Dependent Adolescents (N=84)	Difference Between Non-Dependent and Cannabis Dependent Adolescents ^a	t	p	Difference Between Non-Dependent and Cannabis Dependent Adolescents After Controlling for Age 5 IQ ^a		
							t	p
Full sample								
Age 12 Matrix Reasoning Subtest	10.10	9.29	-0.81	-2.44	.015	-0.39	-1.25	.21
Age 18 Matrix Reasoning Subtest	10.07	9.25	-0.82	-2.48	.014	-0.51	-1.60	.11
Change in Subtest Score ^b	-0.03	-0.04	-0.01	-0.04	.97	-0.11	-0.34	.73
Discordant Twins	Non-Dependent Twins (N=57)	Cannabis Dependent Co-Twin (N=57)	Difference Between Discordant Twin Pairs ^a	t	p	Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a		
							t	p
Age 12 Matrix Reasoning Subtest	9.45	9.02	-0.43	-0.96	.34	-0.47	-1.04	.30
Age 18 Matrix Reasoning Subtest	9.00	8.90	-0.10	-0.20	.84	-0.16	-0.31	.76
Change in Subtest Score ^b	-0.45	-0.12	0.33	0.58	.56	0.32	0.55	.58

Note. Means and statistical tests are adjusted for sex. a. Negative scores indicate that adolescents with cannabis dependence showed lower IQ/greater IQ decline than non-dependent adolescents. b. Change in the Matrix Reasoning subtest score was represented as a change score (age 18 Information – age 12 Information). We focused on subtest decline from age 12 to 18 because the age 12 and age 18 IQ tests were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 IQ test was based on different subtests (Vocabulary and Block Design). Results are shown with and without adjustment for age 5 IQ. Statistically significant differences are shown in bold.

Supplemental Table 6. Mean pro-rated IQ scores at ages 5, 12, and 18 and IQ subtest scores at ages 12 and 18. Means are shown for adolescents who did not use cannabis in the past year at age 18 and adolescents who used cannabis on a weekly or greater basis at age 18. Means for IQ change represent average within-individual IQ change.

Pro-Rated Full Scale IQ								
	Non-User (N=1242)	Weekly+ User (N=132)	Difference Between Non- Users and Weekly+ Users ^a	t	p	Difference Between Non- Users and Weekly+ Users After Controlling for Age 5 IQ ^a	t	p
Full sample								
Age 5 IQ	100.17	95.94	-4.23	-2.91	.004	-	-	-
Age 12 IQ	100.91	94.31	-6.60	-5.21	<.001	-4.40	-4.08	<.001
Age 18 IQ	101.11	92.99	-8.12	-6.53	<.001	-6.13	-5.57	<.001
IQ Change From Age 12-18 ^b	0.20	-1.32	-1.52	-1.43	.15	-1.73	-1.64	.10
	Non-User (N=23)	Weekly+ User (N=23)	Difference Between Discordant Twin Pairs ^a	t	p	Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a	t	p
Discordant Twins								
Age 5 IQ	97.46	98.27	0.81	0.18	.86	-	-	-
Age 12 IQ	94.49	101.15	6.66	1.83	.07	6.39	1.91	.06
Age 18 IQ	94.74	98.13	3.39	0.82	.42	3.02	0.83	.41
IQ Change From Age 12-18 ^b	0.25	-3.02	-3.27	-0.95	.35	-3.37	-0.98	.33
Information Subtest								
	Non-User (N=1242)	Weekly+ User (N=132)	Difference Between Non- Users and Weekly+ Users ^a	t	p	Difference Between Non- Users and Weekly+ Users	t	p
Full Sample								

						After Controlling for Age 5 IQ ^a		
Age 12 IQ	10.16	8.76	-1.40	-5.49	<.001	-0.96	-4.34	<.001
Age 18 IQ	10.24	8.44	-1.80	-7.79	<.001	-1.40	-6.72	<.001
IQ Change From Age 12-18 ^b	0.08	-0.32	-0.40	-1.95	.05	-0.44	-2.09	.037
			Difference Between Discordant Twin Pairs ^a			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a		
Discordant Twins	Non-User (N=23)	Weekly+ User (N=23)		t	p		t	p
Age 12 IQ	8.76	10.10	1.34	1.91	.06	1.31	1.90	.06
Age 18 IQ	9.15	10.24	1.09	1.48	.15	1.05	1.47	.15
IQ Change From Age 12-18 ^b	0.39	0.14	-0.25	-0.38	.70	-0.25	-0.38	.70

Matrix Reasoning Subtest

						Difference Between Non- Users and Weekly+ Users After Controlling for Age 5 IQ ^a		
			Difference Between Non- Users and Weekly+ Users ^a					
Full Sample	Non-User (N=1242)	Weekly+ User (N=132)		t	p		t	p
Age 12 IQ	10.15	9.33	-0.82	-3.32	<.001	-0.50	-2.23	.026
Age 18 IQ	10.12	9.33	-0.79	-2.75	.006	-0.55	-2.00	.046
IQ Change From Age 12-18 ^b	-0.03	0.00	0.03	0.11	.91	-0.05	-0.17	.87
			Difference Between Discordant Twin Pairs ^a			Difference Between Discordant Twin Pairs After Controlling for Age 5 IQ ^a		
Discordant Twins	Non-User (N=23)	Weekly+ User (N=23)		t	p		t	p

Age 12 IQ	9.37	10.34	0.97	1.28	.21	0.91	1.33	.19
Age 18 IQ	9.10	9.06	-0.04	-0.04	.97	-0.13	-0.15	.88
IQ Change From Age 12-18 ^b	-0.27	-1.28	-1.01	-1.16	.25	-1.04	-1.20	.24

Note. Means and statistical tests are adjusted for sex. a. Negative scores indicate that adolescents who used cannabis at least weekly showed lower IQ/greater IQ decline than adolescents who did not use cannabis in the past year. b. IQ change was represented as a change score (age 18 IQ – age 12 IQ). We focused on IQ decline from age 12 to 18 because the age 12 and age 18 pro-rated IQ scores were based on the same two subtests (Information and Matrix Reasoning) whereas the age 5 pro-rated IQ scores were based on different subtests (Vocabulary and Block Design). Results are shown with and without adjustment for age 5 IQ. Statistically significant differences are shown in bold.

Supplemental Table 7. Mean executive function scores for adolescents who did not use cannabis in the past year at age 18 and adolescents who used cannabis weekly or more in the past year at age 18.

Executive Functions	Full Sample								Discordant Twins							
	Before Controlling for Age 12 IQ				After Controlling for Age 12 IQ				Before Controlling for Age 12 IQ				After Controlling for Age 12 IQ			
	Non-User (N=1,242)	Weekly User (N=132)	t	p	Non-User (N=1,242)	Weekly User (N=132)	t	p	Non-User (N=23)	Weekly User (N=23)	t	p	Non-User (N=23)	Weekly User (N=23)	t	p
RVP A Prime	0.06	-0.28	-3.85	<.001	0.04	-0.11	-1.74	.08	0.02	0.12	0.37	.71	0.08	0.06	-0.08	.94
RVP Total False Alarms ^a	-0.03	0.03	0.71	.48	-0.02	-0.07	-0.55	.58	-0.05	-0.31	-0.98	.34	-0.05	-0.30	-0.93	.36
SWM Total Errors ^a	-0.07	0.29	3.91	<.001	-0.05	0.14	2.33	.020	0.02	-0.12	-0.79	.44	-0.05	-0.05	-0.04	.97
SWM Strategy ^a	-0.05	0.28	3.98	<.001	-0.03	0.14	2.19	.029	0.14	0.08	-0.24	.81	0.04	0.18	0.55	.59
Spatial Span Forward	0.06	-0.48	-5.95	<.001	0.04	-0.33	-4.43	<.001	-0.10	-0.07	0.14	.89	0.00	-0.16	-0.75	.46
Spatial Span Reversed	0.07	-0.42	-5.49	<.001	0.05	-0.27	-4.01	<.001	0.14	-0.29	-1.80	.09	0.14	-0.29	-1.91	.07

Note. Means and statistical tests are adjusted for sex. Non-user=did not use cannabis in the past year at age 18. Weekly User=used cannabis weekly or more in the past year at age 18. RVP=Rapid Visual Processing. SWM=Spatial Working Memory. For the full sample, Ns ranged from 1238-1242 for the non-user group and 130-132 for the user group, as a few people from each group did not complete all executive function tests. For discordant twins, N=23 twin pairs. a. Higher scores are worse. Statistically significant differences are shown in bold.